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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/156,367	09/17/98	LIU	Y	YFL98-01PA

HM12/1006

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EXAMINER	
ALLEN, M	

ART UNIT	PAPER NUMBER
1645	4

DATE MAILED: 10/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/156,367	Liu
Examiner	**Group Art Unit**
Marianne P. Allen	1645

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-43* is/are pending in the application.

Of the above, claim(s) *33-43* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-32* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-32, drawn to methods of screening/assessment, classified in at least class 435, subclass 15, for example.

II. Claims 33-43, drawn to methods of treatment, classified in at least class 514, subclass 12, for example.

The inventions are distinct, each from the other because: The methods of Groups I and II can be shown to be distinct, each from the other, because they have different method steps, starting materials, and goals. Upon further consideration, claims 33-35 have been included with group II because the steps involve administration to the mammal and thus are essentially treatment claims.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and the necessity for non-coextensive literature searches, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ms. Alice Carroll on 9 September 1999, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-32. Affirmation of this election must be made by applicant in responding to this Office action. Claims 33-43 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Applicant is being given benefit to the instant filing date (9/17/98) and being denied benefit to the provisional application filing date (5/14/98). As presently written, the full scope embraced by each claim was not disclosed in the provisional application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1-2, 4, 6, 8-9, 11, 13-15, and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al. (Society for Neuroscience Abstracts, October 1997).

Liu et al. is valid prior art under 102(a) as it is authored by other than the named inventive entity.

Liu et al. teaches that expression of the huntingtin mutant activates JNK/APK and induces neuronal apoptosis in hippocampal cells. Dominant-negative SEK(K-R) inhibits this induced apoptosis and may be a therapeutic tool in Huntington's Disease. As such, the abstract fairly teaches the claimed methods for assessing a compound's ability to prevent neuronal death.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-10, 14, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al.

Liu et al. is applied as above but does not specifically identify the hippocampal cell line used. As indicated in the specification at page 9, the HN33 hippocampal cell line would have been well known to those of ordinary skill in the art and it would have been obvious to use this cell line in the method of Liu et al. as a mere matter of substitution.

Claims 1-2, 5-9, 12-16, and 19-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Yardin et al. (Neuroreport, 22 June 1998), Ni et al. (U.S. Patent No. 5,840,509), and Johnson (U.S. Patent No. 5,854,043).

Yardin et al. discloses contacting the drugs FK506 and cyclosporine A with rat cortical cell cultures which are c-Jun positive sympathetic neurons and determining the level of apoptosis following serum deprivation. The level of c-Jun was determined using immunohistochemistry. Cyclosporine A was unable to antagonize the apoptotic effect of serum deprivation. FK506 was known to protect neurons from excitotoxicity in experimental animals. (See at least abstract, Figure 2.)

Ni et al. discloses that apoptosis (cell death) is associated with neurological conditions and that understanding the cellular events resulting or preventing apoptosis would be useful for identifying therapeutic agents to treat such neurological conditions. (See abstract and column 7, lines 40-60.)

Johnson discloses well known methods of evaluating compounds capable of regulating signal transduction in cells, particularly Jun and JNK. Therapeutic applications of such compounds in neuronal disease, for example, are disclosed. (See columns 51-54.)

It would have been obvious to use the experimental system of Yardin et al. to assess a compound's ability to prevent neuronal cell death in neurological conditions. Apoptosis would have been well known to be involved in particular conditions such as Alzheimer's disease and the prior art teaches the association between c-Jun and apoptosis. It would have been further obvious to perform similar assays for apoptosis and c-Jun in the well known excitotoxicity systems disclosed by Yardin et al. in view of this association. The prior art of record establishes that glutamate, quinolinic acid, and kainic acid would have been well known and routinely used excitotoxins. Johnson, Yardin et al., and Ni et al. make clear that it would have been well known how to manipulate various aspects of the second messenger systems to evaluate inhibitors and inducers of apoptosis, enzymatic activity, gene expression, and so forth in the cascade, using well known techniques. (See also Eilers et al., Journal of Neuroscience, 1 March 1998; Herdegen, Journal of Neuroscience, 15 July 1998; and Virdee et al., Journal of Neurochemistry, 1997 for additional evidence that these techniques would have been well known.)

Claims 1-2, 5-7, 9, 12, 14-16, 19-22, and 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Cheung et al. (Journal of Neuroscience Research, 1 April 1998), Ni et al. (U.S. Patent No. 5,840,509), and Johnson (U.S. Patent No. 5,854,043).

Ni et al. and Johnson are applied as above.

Cheung et al. discloses exposing cerebellar granule cells to the excitotoxin kainate and evaluating its effects on apoptosis and c-Jun by in situ hybridization and immunohistochemistry. Other drugs such as CNQX were added to the system to evaluate their inhibitory effects.

It would have been obvious to use the experimental system of Cheung et al. to assess a compound's ability to prevent neuronal cell death in neurological conditions. Apoptosis would have been well known to be involved in neurological conditions and the prior art teaches the association between c-Jun and apoptosis. Johnson, Cheung et al., and Ni et al. make clear that it would have been well known how to manipulate various aspects of the second messenger systems to evaluate inhibitors and inducers of apoptosis, enzymatic activity, gene expression, and so forth in the cascade, using well known techniques. (See also Eilers et al., Journal of Neuroscience, 1 March 1998; Herdegen, Journal of Neuroscience, 15 July 1998; and Virdee et al., Journal of Neurochemistry, 1997 for additional evidence that these techniques would have been well known.)

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Goodenough et al. (Society for Neuroscience Abstracts, October 1997) discloses that administration of the excitotoxin spermine into the striatum causes an elevation of c-Jun mRNA. It had no effect in the hippocampus.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen, whose telephone number is (703) 308-0666. The examiner can normally be reached on Monday-Friday from 9:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached on (703) 308-3995. Official FAX communications may be directed to either (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800
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